Complete Summary

GUIDELINE TITLE

Menopause: a guide to management.

BIBLIOGRAPHIC SOURCE(S)

Brigham and Women's Hospital. Menopause: a guide to management. Boston (MA): Brigham and Women's Hospital; 2005. 15 p. [23 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Menopause
- Menopausal symptoms, such as hot flashes, night sweats, genitourinary symptoms
- Withdrawal bleeding as an adverse event of hormone replacement therapy

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide physicians with clear guidelines for the management of menopause

TARGET POPULATION

Perimenopausal and postmenopausal women

INTERVENTIONS AND PRACTICES CONSIDERED

1. Discussing the risks of hormone replacement therapy (HRT) with patients
2. HRT including estrogens (oral, transdermal, and vaginal); progestins; and estrogen-progestin combinations (refer to Table 4 in the original guideline document for details)
3. Low-dose oral contraceptives for perimenopausal women
4. Alternatives to HRT (refer to Table 5 in the original guideline document)
5. Endometrial biopsy or transvaginal endometrial ultrasound, if indicated

MAJOR OUTCOMES CONSIDERED

Benefits and adverse events of hormone replacement therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches using Medline.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Who Should Be Considered for Hormone Replacement?

In light of the Women's Health Initiative (WHI) data (refer to the original guideline document for details on the WHI study), the only indication for starting hormone replacement therapy (HRT) is for the treatment of moderate-severe hot flashes or other vasomotor symptoms. Although HRT has been

shown to be effective in increasing bone density and reducing fractures, it is not recommended as a first-line treatment for osteoporosis, given the risks of therapy and the availability of suitable and effective alternative anti-resorptive drugs. Genitourinary symptoms can be treated by topical vaginal estrogen preparations, and these would be the first-line treatments for this indication (see Table 4 in the original guideline document).

In light of the findings from the Women's Health Initiative, HRT should not be prescribed for the purpose of reducing cardiac risk.

Who Should NOT Use HRT?

See the "Contraindications" field for absolute and relative contraindications to HRT.

HRT Regimens

If the decision to begin HRT is made, to control hot flashes, the following considerations are important.

When to Use Unopposed Estrogen versus Estrogen/Progestin Combination Therapy

Women who have had a hysterectomy may receive unopposed estrogen. There is no reason to add a progestin to estrogen in women without a uterus. Women with an intact uterus should always receive estrogen in conjunction with a progestin to avoid the risk of endometrial hyperplasia.

Short-Term versus Long-Term HRT

Short-term HRT is a reasonable strategy for patients with disabling hot flashes. HRT should be initiated in these patients, with a full explanation as to the risks. (In the WHI, patients were only on HRT for an average follow-up time of 5.2 years, in which time there were small but statistically significant increases in adverse effects.) Discussions about discontinuation should occur at regular intervals.

Although long-term use of HRT is not recommended, some patients decide to continue it, in spite of information about adverse effects. If adverse effects do occur (deep venous thrombosis, myocardial infarction [MI], stroke, breast cancer), therapy should be discontinued.

Combination Therapy: When to Use Cyclical versus Continuous HRT

When combined therapy is used, the progestin may be prescribed cyclically or continuously. In the cyclical regimen, estrogen is given daily (either orally or transdermally) and a progestin is added for days 1-14 of each month. Shorter durations of progestin therapy are associated with an increased incidence of endometrial hyperplasia. The cyclical method results in monthly bleeding, usually occurring at the end of the progestin administration. This method is advised for women who are recently menopausal. For women who tolerate progestins poorly,

daily estrogen combined with a 14-day course of 10 mg medroxyprogesterone acetate [MPA] daily every three-month cycle is a reasonable alternative regimen.

With a continuous regimen, women are given estrogen and low-dose progestin (e.g., 2.5 mg MPA) daily. With this method, within 9 to 12 months, in about 75% of women the endometrium will become atrophic and vaginal bleeding will cease. It is important to note that bleeding can occur in an irregular, unpredictable fashion until the end of the first year. If excessive bleeding occurs (heavier than patient's past or usual periods) with the continuous regimen, or if bleeding occurs before day 6 of progestin on the cyclical regimen, endometrial biopsy should be considered.

Transdermal Estrogens

Transdermal estrogens have the advantage of no "first-pass" through the liver. Therefore, this form of estrogen does not substantially increase levels of clotting factors or triglycerides.

There have been no large-scale randomized controlled trials of transdermal estrogen in combination with a progestin. In the WHI study, combination oral premarin/provera (Prempro) was used. Switching patients from oral combined premarin/provera to transdermal estrogen in combination with a progestin for the express purpose of avoiding the adverse effects of HRT noted in the WHI is not recommended.

How Should HRT Be Initiated?

For patients who are perimenopausal (still menstruating, often irregularly, and experiencing vasomotor symptoms), low-dose oral contraceptives may be used for one to two years (contraindicated in smokers). At that point, if a woman is still experiencing severe hot flashes, she can be switched to cyclical HRT. If excessive bleeding occurs, the patient can be restarted on oral contraceptive pills for an additional year, and then switched to HRT. If bleeding is irregular or excessive, consider referring the patient to a gynecologist. Starting HRT while women are still menstruating or recently menopausal (within 6 months) leads to unpredictable estrogen levels and irregular bleeding, and is therefore not recommended.

How Should HRT Be Stopped?

Since the publication of the WHI study, it is generally believed that the risks of long-term HRT or estrogen replacement therapy (ERT) outweigh the benefits. Given that there is some (very low) risk of adverse events, women who are taking HRT for reasons other than control of postmenopausal symptoms should be encouraged to stop. HRT may be stopped "cold turkey" or with a slow taper, although there are no data comparing the efficacies of the two different strategies.

Management of Abnormal Bleeding Patterns on HRT

When Is an Endometrial Biopsy Indicated for Patients Taking HRT?

- Patients on cyclical HRT with unscheduled bleeding or bleeding before day 6 of progestin
- Patients on continuous HRT with bleeding after six to nine months of use
- Patients who have bleeding after a sustained period of amenorrhea
- Patients on the continuous regimen who have excessive bleeding (heavier than patient's past period). If the biopsy reveals only a proliferative endometrium, the dose of estrogen can be increased (5 mg MPA daily), or the patient can be switched to the cyclical regimen.

Alternative to Endometrial Biopsy

Instead of an endometrial biopsy, a transvaginal endometrial ultrasound may be done. Using 5 mm of endometrial thickness as a cutoff, this test has a negative predictive value of 99% in women on combined HRT. However, about 25 to 50% of women on HRT will have an endometrial thickness > 5mm. All these women should have an endometrial biopsy.

For women who have a uterus and who are taking unopposed estrogen (not recommended, as noted above), the test is poor (positive predictive value of 12%), since the endometrium usually thickens in this setting. This test is highly dependent on the skill of the ultrasonographer.

Absence of Bleeding

Many women who have been on cyclical HRT for many years will not experience withdrawal bleeding, and this is not considered abnormal. Moreover, women who start HRT many years after menses have stopped also may experience no withdrawal bleeding.

Guideline Summary

- Moderate-to-severe vasomotor (hot flashes, night sweats) and genitourinary symptoms that are unresponsive to topical agents are the primary indications for oral estrogen use. HRT should be used short-term only.
- Data from the WHI and HERS trials have shown that HRT has no role in the primary or secondary prevention of cardiovascular disease in postmenopausal women.
- HRT is associated with increased risks of stroke and venous thromboembolic events.
- HRT use is not associated with improvements in cognition or reduction in dementia.
- Combination estrogen + progestin HRT use, even for 5 years or less, is associated with an increased risk of breast cancer.
- Although HRT does increase bone density and reduces fracture risk, it is not recommended as a first line treatment for osteoporosis because of adverse effects.
- If a patient chooses HRT, risks of therapy should be addressed at regular intervals as additional data become available.

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for Initiation and Monitoring of Short-Term HRT Therapy and Management of Patients on Long-Term HRT

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

Guidelines are based on a comprehensive assessment of recent literature on hormone replacement therapy.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of hormone replacement therapy (HRT)
- Appropriate management of abnormal bleeding patterns on HRT
- Relief of hot flashes in peri and post-menopausal women

POTENTIAL HARMS

Hormone replacement therapy (HRT) is associated with an increased risk of adverse events, including fatal and non-fatal coronary events, strokes, clots, and breast cancer.

The most common side effects of estrogen:

- Nausea
- Headaches
- Breast tenderness
- Vaginal bleeding

Adverse effects associated with progestins:

- Breast tenderness
- Weight gain
- Edema
- Pre-menstrual (PMS)-like syndromes
- Depression
- Irritability

CONTRAINDICATIONS

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Absolute Contraindications to Hormone Replacement Therapy (HRT)

The following groups of women should not receive HRT, even if they have intolerable hot flashes

- Women with vaginal bleeding of unknown etiology
- Breast cancer survivors: Somewhat controversial. American College of Obstetrics and Gynecology report from 1994 recommends use with caution, if indicated, but American College of Physicians states risks may outweigh benefits in this group. Few randomized controlled trial data are available to help make this decision.
- Patients with active liver disease
- History of endometrial cancer (Stage II or greater, or Stage I with deep invasion and positive nodes; may be used in women with a history of Stage I endometrial cancer with no endometrial or myometrial invasion)
- History of venous thromboembolic disease (deep vein thrombosis [DVT] or pulmonary embolism [PE])
- Known coronary heart disease (CHD)

Relative Contraindications to HRT

- Active gall bladder disease. Transdermal estrogen preferable if decision is made to use hormonal therapy
- History of migraine headaches
- Elevated serum triglycerides (>400)
- Strong family history of breast cancer (more than one first degree relative affected)
- History of fibroids
- Atypical ductal hyperplasia of the breast

The use of low-dose oral contraceptives is contraindicated in smokers.

QUALIFYING STATEMENTS

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- This guide is not intended to convey rigid standards. Instead, it should be tailored to the needs of each individual woman.
- The mean age of participants in the Women's health Initiative (WHI) was 63 years old. Since younger postmenopausal women (50-54 years) were a small minority of the WHI, and women who were committed to taking estrogen replacement therapy (ERT) or hormone replacement therapy (HRT) were not enrolled, findings on quality of life are not clearly generalizable to this group. Women below age 50 were not included in the WHI, and the findings cannot be generalized to women with premature menopause to this group of patients. Standard practice is to start women with premature ovarian failure on oral contraceptive pills.
- Data from the WHI did not reveal a significant increase in the incidence of ovarian cancer in women on combined estrogen-progestin therapy. A cohort study has also suggested an increased risk of ovarian cancer in women on estrogen alone, especially those taking it for 10 or more years.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Brigham and Women's Hospital. Menopause: a guide to management. Boston (MA): Brigham and Women's Hospital; 2005. 15 p. [23 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005

GUIDELINE DEVELOPER(S)

Brigham and Women's Hospital (Boston) - Hospital/Medical Center

SOURCE(S) OF FUNDING

Brigham and Women's Hospital

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Brigham and Women's Hospital Web site.

Print copies: Available from the Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115. Telephone: (800) BWH-9999.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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